

Nipple candidiasis among breastfeeding mothers

Case-control study of predisposing factors

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OBJECTIVE To investigate factors that predispose breastfeeding mothers to nipple candidiasis.

DESIGN A retrospective case-control study of women attending the Calgary Breastfeeding Clinic.

SETTING Ambulatory breastfeeding referral centre.

PARTICIPANTS All women (105) who attended the clinic during a 3.5-month study period. All were referred for problems with breastfeeding; 27 (the case group) had positive diagnostic criteria for nipple candidiasis. The other 78 formed a control group.

MAIN OUTCOME MEASURE A patient information sheet, completed while taking a medical history, recorded the presence or absence of four possible predisposing factors. Two infant variables were also noted on physical examination. Patients were diagnosed as having or not having nipple candidiasis on the basis of specific clinical criteria, and statistics on other variables were compared for those with positive and with negative diagnoses.

RESULTS A statistically significant correlation ($P < 0.05$) was found between nipple candidiasis and three factors: vaginal candidiasis ($P = 0.001$), previous antibiotic use ($P = 0.036$), and nipple trauma ($P = 0.001$).

CONCLUSIONS Further research is required to establish clear causality. However, we recommend that physicians be suspicious of nipple candidiasis; avoid antibiotics or use the shortest effective course; treat yeast vaginitis during the third trimester and after delivery aggressively; and treat mothers for nipple yeast if babies have oral or diaper candidiasis. Breastfeeding mothers can also be counseled in preventive measures.

OBJECTIF Investiguer les facteurs qui prédisposent les mères allaitantes à la candidose du mamelon.

CONCEPTION Étude rétrospective de cas-témoins auprès des femmes fréquentant la clinique d'allaitement de Calgary.

CONTEXTE Centre ambulatoire de référence pour l'allaitement.

PARTICIPANTES Toutes les femmes (105) qui ont fréquenté la clinique pendant les 3,5 mois de la période d'étude. Elles avaient toutes été référées pour des problèmes d'allaitement. Parmi celles-ci, 27 (le groupe de cas) répondaient aux critères diagnostiques positifs d'une candidose du mamelon. Les 78 autres ont constitué le groupe témoin.

PRINCIPALES MESURES DES RÉSULTATS Sur une feuille de renseignements concernant la patiente, on inscrivait la présence ou l'absence de quatre facteurs prédisposants potentiels. À l'examen physique, on notait également deux variables reliées au nourrisson. Le diagnostic positif ou négatif de candidose du mamelon reposait sur quatre critères cliniques spécifiques. On a comparé les statistiques concernant les autres variables entre les diagnostics positifs et les diagnostics négatifs.

RÉSULTATS L'analyse a révélé une corrélation statistiquement significative ($p < 0,05$) entre la candidose du mamelon et trois facteurs: candidose vaginale ($p = 0,001$), antibiothérapie antérieure ($p = 0,036$) et traumatisme du mamelon ($p = 0,001$).

CONCLUSIONS Il est nécessaire de poursuivre les recherches pour établir clairement un lien de causalité. Nous recommandons toutefois d'être vigilants face à la candidose du mamelon: éviter les antibiotiques ou utiliser le traitement efficace le plus court possible, traiter agressivement la candidose vaginale pendant le troisième trimestre ou après l'accouchement et traiter les mères contre la candidose du mamelon si les nourrissons présentent une candidose orale ou un érythème fessier à champignons. On peut également donner des conseils sur les mesures préventives aux mères qui allaitent.

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Table 1. Patient data

Have you had a previous vaginal yeast infection?

Have you been taking antibiotics?

- During pregnancy? What was the reason and the timing?
- At delivery? What was the reason and the timing?
- After delivery? What was the reason and the timing?

Have you had any injury to your nipple while establishing breastfeeding?

Do you have diabetes (gestational, insulin-dependent, or non-insulin-dependent)?
Has anyone in your family had diabetes?

What have you been eating?
Have you had any changes to your diet? What do you feed your infant? Have there been any changes to the diet?



CANDIDA INFECTIONS HAVE BEEN reported in virtually every tissue in the human body, although by far the most common manifestations of candidiasis are superficial lesions, especially infections of the mucous surfaces of the mouth and vagina.¹ *Candida* does not usually colonize healthy glabrous skin, such as the nipple. It can do so, however, during lactation, causing pain and erythema.

Nipple candidiasis is characterized by severe burning pain, as well as stabbing pain, which often radiates throughout the breast and is typically worse after feedings.²⁻⁶ Pain and discomfort can lead to the early cessation of breastfeeding if the infection is not recognized promptly and treated appropriately.

Few researchers have investigated the factors that predispose nursing mothers to nipple candidiasis, although an association between oral thrush in infants and nipple thrush in mothers has been reported.^{2,7,8} Early studies showed that cases of oral infection in term babies within the first few days of life are caused primarily by maternal contamination of the newborn during delivery.⁸⁻¹⁰ *Candida* can be present in the mother's vagina either symptomatically or asymptotically. Vaginal yeast infection has been shown to increase during pregnancy.¹¹

It is probable, however, that some other factor alters the host's defences and allows yeast to colonize the nipple at pathological levels. Several conditions have been suggested, including nipple trauma, diet, diabetes, corticosteroids, and antibiotic therapy.¹² For example, several reports have described colonization of nipple fissures by *Candida*.^{6,13,14} But much of the literature is anecdotal; very few studies have examined which of these factors correlate with nipple yeast.

The most complete study to date is by Amir,¹² who attempted to identify predisposing factors among women attending the Family Planning Association in Victoria, Australia.

Amir's findings suggested a correlation between nipple candidiasis and several factors, primarily nipple damage in early lactation, use of antibiotics after delivery, previous long-term antibiotic use, and previous vaginal yeast infection. The study lacked clear diagnostic criteria, however, and the cases and controls were recruited from different patient populations. Further research is thus required to confirm Amir's findings.

Our study aimed to investigate factors that could predispose breastfeeding mothers to nipple candidiasis. Women attending the Calgary Breastfeeding Clinic were surveyed at the time of consultation. The patients attending the clinic had all been referred because they were having problems with breastfeeding. This population, therefore, had a high concentration of nipple candidiasis: 25%. The retrospective case-control approach yielded a larger number of cases than would have been available in a prospective study.

METHODS

Sample population

Information was gathered from all patients attending the Calgary Breastfeeding Clinic from the beginning of January to mid-April, 1992. The women were asked by the nurse lactation consultant in the clinic whether they would like to participate in the study; all 105 of them signed the consent form.

Patients had been referred by their primary care physicians. The provincial health insurance plan covered all the services. The main reason for attending the clinic was painful breastfeeding. Other reasons included latching difficulties, inverted nipples, infants failing to thrive, and problems with milk supply. The case group was comprised of all the women (n = 27) who fulfilled the diagnostic criteria for nipple candidiasis. The control group was made up of all the women attending

the clinic during the study period who did not meet the criteria for nipple candidiasis ($n = 78$).

Research protocol

During the medical history, a patient information sheet containing questions on the presence or absence of several variables was completed (Table 1).

Four different categories of putative predisposing factors were investigated: previous yeast infection, antibiotic use during the pregnancy or during the postnatal period, nipple trauma, and gestational diabetes. Patients were then given a physical examination and diagnosed as positive or negative for nipple candidiasis.

Criteria for diagnosis

Nipple candidiasis was diagnosed solely on clinical grounds. A clinical diagnosis was chosen over culture because it has been demonstrated that, for *Candida* infections of the vagina, no relation is found between the number of *Candida* organisms isolated and the presence of vaginal symptoms,¹⁵ whereas aggregate symptoms had a high sensitivity, specificity, and predictive value.¹⁶ Extensive clinical experience of one of the authors suggested that the same held true for nipple candidiasis.

Patients were diagnosed with nipple candidiasis if they presented with all three of the following²⁻⁶:

- Severe, burning nipple and areolar pain that is worse after feedings and lasts for at least 15 minutes or for the entire period between feedings. Onset is later than the first postpartum week. If yeast infection supervenes in a mother with painful nipples resulting from trauma caused by poor latching of the baby, the nature of the pain will change to the distinct pattern of burning pain after feeding. Pain from candidiasis, unlike pain from trauma, does not respond to improving the nursing technique;
- Deep, shooting pains radiating into the breast tissue, which occur during and between feedings; and

- Red or purple discoloration of the nipple and proximal areola.

Other signs that occur frequently, but that we did not use as diagnostic criteria, include a sheen on the affected areola, mild edema of the areola, and fine circumferential cracks around the nipple. An infrequent finding is white spots on the nipple that appear curdy, like cottage cheese.

Candidiasis infection in the infant

Data were also collected on two other variables that are reported to be associated with nipple candidiasis: the presence of oral thrush and *Candida* diaper

Table 2. Factors that could predispose women to nipple candidiasis

PREDISPOSING FACTOR	CASES (N = 27)	CONTROLS (N = 78)	P LEVEL*
Vaginal candidiasis	22 (81%)	35 (45%)	0.001
Previous antibiotics	14 (52%)	23 (29%)	0.036
Nipple trauma	19 (70%)	24 (31%)	0.001
* χ^2 analysis.			

rash in the infant (at the time of physical examination in the clinic).

Ethics

Procedures were in accordance with the ethical standards of the Medical Ethics Committee of the University of Calgary.

Statistics

Percentages, χ^2 , and probabilities were calculated using Mystat (Systat, Inc, Evanston, Ill). The required level for statistical significance was $P < 0.05$.

RESULTS

A statistically significant correlation ($P < 0.05$) was found between nipple candidiasis and three of the putative

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predisposing factors: vaginal candidiasis, nipple trauma, and previous use of antibiotics (Table 2). The prevalence of gestational diabetes was too low to make any reliable deductions. Dietary factors were too complex to permit any conclusions to be drawn.

Table 3. Temporal relationship between antibiotic use and nipple candidiasis

TIME BEFORE DIAGNOSIS	CASES	CONTROLS
During pregnancy	3	12
After delivery		
• <2 weeks	1	5
• 2-4 weeks	8	3
• >4 weeks	1	1
• Unknown	1	2
TOTAL	14	23

Table 4. Concomitant Candida infection in the infant

INFECTION IN THE INFANT	CASES (N = 27)	CONTROLS (N = 78)
Visible oral thrush	9 (33%)	0 (0%)
Diaper candidiasis	13 (48%)	0 (0%)

Vaginal candidiasis

Although many of the women in both groups reported previous vaginal yeast infections at some time in their lives, a significantly higher percentage of the group with nipple candidiasis reported previous vaginal yeast infections ($P = 0.001$).

Nipple trauma

There was also a strong association between nipple trauma and the subsequent development of nipple yeast infection. Seventy percent of the case group reported sore, cracked nipples before developing the distinct symptoms of nipple candidiasis as compared with only 31% of the control group ($P < 0.001$).

Use of antibiotics

Of the 105 women participating in the study, 37 reported taking antibiotics at some time during the prenatal or postnatal periods. Antibiotics had been taken for several reasons, including urinary tract infections, upper respiratory tract infections, mastitis, and acne. A significantly higher percentage of women in the case group than in the control group had taken antibiotics ($P = 0.036$). Nineteen percent of the case group and 6% of the control group reported taking antibiotics for mastitis. The timing of antibiotic use was even more suggestive: 41% of the cases had received antibiotics in the postnatal period compared with 14% of the control subjects. Of women taking antibiotics after delivery, 73% of the case group reported taking antibiotics within 2 to 4 weeks of being diagnosed with nipple candidiasis (8/11, Table 3) whereas only 27% (3/11) of the women in the control group fell into the same time interval.

Candida in infants

None of the infants in the control group had a clinical diagnosis of oral thrush or diaper candidiasis, whereas 48% of the infants in the case group had diaper yeast and 33% had visible oral thrush (Table 4).

DISCUSSION

Validity of the study

Misclassification of the subjects into "case" and "control" groups has been minimized by defining, a priori, strict clinical criteria for the diagnosis of nipple candidiasis. In contrast to Amir's study,¹² we gathered data directly through in-person questionnaires from both the case and control groups. Moreover, all the control subjects attended the same clinic as the cases. The very high rate of consent probably reflects the strong motivation of these women. While, by definition, they represent a statistically select group, this should not detract from the validity of

the study because the cases and controls came from the same pool of women. Furthermore, we surmise that infected women who do not receive appropriate treatment are likely to stop breastfeeding, often without an established diagnosis.

We are reasonably confident that the correlations between nipple *Candida* infection and these predisposing factors reflect the situation in the population at large. Our findings substantiate preliminary data presented by Amir¹² and provide strong, statistically relevant evidence that these factors predispose to nipple candidiasis.

Antibiotic use

The most important finding of this study – important because it relates to a potentially modifiable factor – is the association between antibiotics and nipple candidiasis. Antibiotics are reported to predispose to *Candida* infections at other sites.^{16,17} When the antibiotics eliminate or reduce the resident bacteria that normally compete with yeast for nutrients, the yeast are able to multiply more readily, and their overgrowth can lead to invasive infection.

Do our data support the idea that antibiotics also predispose to nipple yeast? It is important to establish whether an appropriate temporal relationship exists between the use of antibiotics and the onset of nipple candidiasis. We found that 73% of the women in the case group reported taking antibiotics 2 to 4 weeks before diagnosis, a period consistent with a causal relationship. Although our study does not prove a link between antibiotics and nipple candidiasis, it does provide substantial evidence to support one.

This possible link should be taken into consideration before prescribing antibiotics for mastitis. Nineteen percent (5/27) of the case group had been prescribed antibiotics for mastitis, compared with 6% (5/78) of the control group. While antibiotics are an accepted treatment for this condition,

alternative therapies, such as massage, rest, milk expression, and increased nursing on the affected breast, often effectively resolve mastitis.⁵

Furthermore, the possibility of a link between mastitis, antibiotics, and the subsequent development of nipple candidiasis would be important to examine in future studies. A prospective study could follow women diagnosed with mastitis who are given either antibiotics or alternative therapies to see what proportions of the two treatment groups develop nipple candidiasis.

Nipple trauma

This study demonstrated a correlation between nipple damage and nipple yeast infection. Odds¹ described trauma or maceration as mechanical factors that predispose to candidiasis. Trauma can provide a route of entry for the microorganism. Although this rationale makes implicit sense, other possible explanations for the association cannot be ruled out. For example, some of the women might have developed cracked nipples as a result of the *Candida* infection and not vice versa. In this study, however, women in the case group reported significantly more nipple trauma while establishing breastfeeding than did women in the control group.

It thus becomes important to prevent trauma and preserve nipple integrity, which also reduces the likelihood of invasion by bacteria or yeast.^{6,12,13} Proper positioning of the infant at the breast and correct latching technique are paramount. Moreover, good technique is basic to comfortable, pain-free nursing. And pain inhibits the milk ejection reflex, which could increase the incidence of plugged ducts and mastitis. Thus, necessary antibiotic treatment could be reduced by giving mothers and babies whatever early assistance they require to establish effective and comfortable breastfeeding. In addition, babies who exhibit such conditions as ankyloglossia, nipple confusion, or incorrect

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Table 5. Measures to prevent nipple candidiasis

WHAT PHYSICIANS CAN DO

Prevention

- Avoid antibiotics unless sound indication.
- Use short courses of antibiotics when needed.
- Consider antifungal nipple cream prophylactically for yeast-prone mother receiving postpartum antibiotics.

Diagnosis

- Diagnose yeast vaginitis if symptoms are present, if clinical appearance is suspect, or if culture is positive.
- Maintain high index of suspicion.

Treatment

- Treat yeast vaginitis in third trimester and postpartum aggressively and prophylactically if antibiotics have been used and patient has a history of yeast vaginitis.
- Treat mother for nipple yeast after delivery if baby has oral or diaper candidiasis.

WHAT PATIENTS CAN DO

Prenatally

- Attend breastfeeding class.
- Report symptoms of yeast vaginitis to physician.

Postpartum

- Seek early assistance in latching.
- Obtain help promptly for nipple trauma.
- Avoid disposable breast pads, which can abrade and occlude.
- Reduce dietary sugar if yeast vaginitis-prone.
- Avoid nipple infection from vagina through good hygiene.
- See physician if nipple pain appears after feeding.

sucking pattern should be identified early so that steps can be taken to avoid nipple trauma.

Vaginal yeast

Although a self-reported history of previous vaginal yeast infection was found to correlate well with the presence of nipple candidiasis, it is difficult to draw firm conclusions because the data on vaginal yeast infection included all cases, regardless of timing of infection; therefore we considered post hoc analysis to be of dubious value. Future studies will concentrate on establishing the timing of the vaginal yeast infections and the other predisposing factors in relation to the nipple *Candida* infection.

Infant infection

Another important finding was the high incidence of oral and diaper candidiasis among infants of mothers with nipple candidiasis. This concurrence of *Candida* infection in mother and baby has been documented previously, although anecdotally.^{1,2,5,12} The generation of statistically significant data, as presented here, has important implications for treating nipple and oral candidiasis. It emphasizes the need to treat both mother and infant with topical antifungal agents even if only one is exhibiting symptoms. Equally important is the teaching of hygiene measures to prevent infection being passed back and forth between mother and infant. In addition, approaches to prevent nipple yeast infection (Table 5) can decrease the incidence of infant oral thrush.

Conclusion

Our results suggest that the natural history of nipple candidiasis, in at least a subset of nursing mothers, involves one or more of the associated predisposing factors: antibiotics, vaginal yeast infection, and nipple trauma. However, further work in this area is required to obtain a clearer understanding of the pathogenesis of nipple candidiasis. Now that these factors have been identified, we can focus on

changes in management of nursing mothers and their infants (Table 5) to see whether the incidence of nipple candidiasis can be reduced. ■

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Naprosyn should not be given to patients with active peptic ulcer or active inflammatory disease of the gastrointestinal tract. It is also contraindicated for those who have shown a sensitivity to it and for patients in whom ASA or other NSAIDs induce the syndrome of asthma, rhinitis or urticaria. Sometimes severe and occasionally fatal anaphylactoid reactions have occurred in such individuals. Suppositories should not be given to patients under 12 years of age or those with inflammatory lesions of the rectum or anus.

WARNINGS

Peptic ulceration, perforation and gastrointestinal bleeding, sometimes severe and occasionally fatal have been reported during therapy with NSAIDs, including Naprosyn.

Naprosyn should be given under close supervision to patients prone to gastrointestinal tract irritation particularly those with a history of peptic ulcer, diverticulosis or other inflammatory disease of the gastrointestinal tract. Patients taking any NSAID should be instructed to contact a physician immediately if they experience symptoms or signs suggestive of peptic ulceration or gastrointestinal bleeding. These reactions can occur without warning at any time during the treatment. Elderly, frail and debilitated patients appear to be at higher risk from a variety of adverse reactions from NSAIDs. For such patients, consideration should be given to a starting dose lower than usual.

The safety of Naprosyn in pregnancy and lactation has not been established and its use is therefore not recommended.

PRECAUTIONS

Naprosyn (naproxen) should not be used concomitantly with the related drug Anaprox (naproxen sodium) since they both circulate in plasma as the naproxen anion.

GI system:

If peptic ulceration is suspected or confirmed, or if gastrointestinal bleeding or perforation occurs, Naprosyn should be discontinued, and appropriate treatment instituted.

Renal Effects: Patients with impaired renal function, extracellular volume depletion, sodium restrictions, heart failure, liver dysfunction, those taking diuretics, and the elderly are at greatest risk of developing overt renal decompensation. Assessment of renal function in these patients before and during therapy is recommended. Naprosyn and its metabolites are eliminated primarily by the kidneys, and therefore, a reduction in daily dosage should be anticipated to avoid the possibility of drug accumulation in patients with significantly impaired renal function.

Peripheral edema has been observed, consequently, patients with compromised cardiac function should be kept under observation when taking Naprosyn. Naprosyn Suspension contains sodium chloride (20 mg/mL). This should be considered in patients whose overall intake of sodium must be restricted.

As with other drugs used with the elderly or those with impaired liver function it is prudent to use the lowest effective dose.

Severe hepatic reactions including jaundice, and cases of fatal hepatitis have been reported with NSAIDs. The prescriber should be alert to the fact that the anti-inflammatory, analgesic

and antipyretic effects of Naprosyn may mask the usual signs of infections. Periodic liver function tests and ophthalmic studies are recommended for patients on chronic therapy. Caution should be exercised by patients whose activities require alertness if they experience drowsiness, dizziness, vertigo or depression during naproxen therapy. Naprosyn may displace other albumin-bound drugs from their binding sites and may lead to drug interactions or interfere with certain laboratory tests. See Product Monograph for further details.

ADVERSE REACTIONS

(1) Denotes incidence of reported reactions between 3% and 9%. (2) Denotes incidence of reported reactions between 1% and 3%. See Product Monograph for reactions occurring in less than 1% of patients.

Gastrointestinal: Heartburn(1), constipation(1), abdominal pain(1), nausea(1), diarrhea(2), dyspepsia(2), stomatitis(2), diverticulitis(2). Rectal burning(1) has been reported occasionally with the use of naproxen suppositories.

Central Nervous System: Headache(1), dizziness(1), drowsiness(1), lightheadedness(2), vertigo(2), depression(2), and fatigue(2).

Skin: Pruritus(1), ecchymoses(1), skin eruptions(1), sweating(2), and purpura(2).

Cardiovascular: Dyspnea(1), peripheral edema(1), and palpitations(2).

Special Senses: Tinnitus(1), and hearing disturbances(2).

Others: Thirst(2).

Adverse reactions reported for SR tablets were similar to standard tablets.

DOSAGE AND ADMINISTRATION

Adult: Oral: The usual total daily dosage for osteoarthritis, rheumatoid arthritis and ankylosing spondylitis is 500 mg (20 mL, 4 teaspoons) a day in divided doses. It may be increased gradually to 750 or 1000 mg or decreased depending on the patient's response. Patients with rheumatoid arthritis or osteoarthritis maintained on a dose of 750 mg/day in divided doses can be switched to a once daily dose of Naprosyn SR 750 mg. The single daily dose of Naprosyn SR should not be exceeded and can be administered in the morning or evening. Naprosyn SR tablets should be swallowed whole.

Rectal: Naprosyn Suppositories (500 mg) can replace one of the oral doses in patients receiving 1000 mg of Naprosyn daily.

Juvenile Rheumatoid Arthritis: The recommended daily dose is approximately 10 mg/kg in two divided doses.

AVAILABILITY

Naprosyn is available as: 250 mg, 375 mg, and 500 mg Tablets, as 250 mg, 375 mg and 500 mg Enteric Coated Tablets, as 750 mg Sustained-Release Tablets and 500 mg Suppositories. Suspension: Each 5 mL contains 125 mg of naproxen. Shake bottle gently before use. Pharmacists are to provide the Naprosyn Patient Information leaflet when dispensing this drug. Product Monograph available to health professionals upon request.

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